ATTACHMENT A
Remarks

Claims 3-4 stand pending in the present application. Upon entrance of the Amendment after Final, Applicants have amended claim 3. Applicants respectfully submit that the present application is in condition for allowance based on the discussion which follows.

As an initial point, it is respectfully submitted that this Amendment after Final should be entered as the amendment to claim 3 makes the claim language more commensurable with the arguments of the previously filed response. Moreover, the amendment to claim 3 more clearly recites the present photodynamic therapy (PDT) method as was interpreted correctly by the Examiner and which the Examiner applied the prior art, namely a PDT method in conjunction with Percutaneous Transluminal Coronary Angioplasty (PTCA).

Furthermore, the amendment to claim 3 does not raise new issues for consideration and no additional prior art search needs to be conducted as any previous prior art search would have covered the subject matter now recited in amended claim 3. This is in accordance with MPEP § 900 which states, in part, that the prior art search should be conducted by the Examiner after obtaining a thorough understanding of the invention disclosed and claimed including the inventive concept to which the claims appear to be directed. The features now recited in independent claim 3 were disclosed in the application as filed. Moreover, the Examiner has examined the claims in accordance with how claim 3 (Currently Amended) is recited. Therefore, in accordance with MPEP § 900, all elements of the currently pending claims have been searched and considered and thus the amendment does not raise new issues for consideration.

Finally, it is respectfully submitted that the amendment to the claims places the application in proper condition for allowance, serves in providing a complete application file history, enhances the clarity of the prosecution record and places the application in condition for appeal. Therefore entrance of the Amendment after Final is proper.

Turning now to the subject matter of the outstanding Final Office Action (hereinafter Office Action), claims 3 and 4 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Aizawa et al (hereinafter Aizawa) in view of Narciso Jr. U.S. Patent No. 5,298,018 (hereinafter Narciso). The Examiner alleges that Narciso teaches PDT during a PTCA procedure to limit restenosis of a blood vessel intima subject to a smooth cell proliferation citing Narciso Abstract. Further, the Examiner alleges that Narciso discloses that the use of a photodynamic agent can be during or after a PTCA procedure, citing Narciso col. 2 lines 60-65. Then, the Examiner concludes that since Narciso teaches the use of a PDT during a PTCA procedure, all method steps of the present claims are inherently disclosed.

Contrary, to the Examiner's allegation, Narciso individually or in combination with Aizawa fails to teach or suggest the present invention. As discussed above, in order to more clearly recite Applicants' invention, Applicants have amended claim 3 to now more clearly recite the claimed PDT method where the PDT therapy is conducted from 0.5-6 hours after the administration of the claimed e6 compound and which compound is administered immediately after the angioplasty treatment. Further, the radiating is conducted at a wavelength of 664 nm and at a laser fluence of 1-10 J/cm^2.

Subject matter basis for the amendment to claim 3 can be found in the Specification as filed and therefore the amendment to claim 3 does not constitute new

matter. For example, the now recited one time administration of the e6 compound and at a dose of 0.1-5 mg/kg is supported in the Specification including Examples 1 and 2 which are specifically directed to a single administration of the mono-L- aspartylchlorin e6 compound at the claimed dosage. The now amended "at a time of 0.5-6 hours after the administration of the photosensitizing compound to commence irradiating" language can found in the Specification as filed on page 14 lines 8-14. Finally, with regard to irradiating at 664 nm, this limitation is found in the Specification as filed on page 14, line 22. With regard to the laser fluence power of 1-10 J/cm^2, support for this limitation can be found in the Specification page 15, lines 4-8 which refers to a laser fluence of 1-100 J/cm^2.

Applicants respectfully submit that the present invention as recited in claim 3 (Currently Amended) is not taught or suggested by the prior art individually or in combination with one another. Aizawa only refers to irradiating using a total energy of 50 J/cm^2 during the intravascular catheterization using a laser-emitting catheter comprising a quartz fiber bundle of 300 microns in the core diameter (Aizawa col. 20, lines 4-20 and lines 35-46) and applying a laser fluence of 50 J/cm^2 the outside of the vessel wall of the branchial artery (see Aizawa col. 21, lines 2-10). Narciso only refers to a laser fluence of 20 J/cm^2 for the laser irradiation for the laser-emitting catheter (Narciso col. 8, lines 65-68 and col. 8, lines 18-33). Accordingly, the now recited laser fluence of 1-10 J/cm^2 is clearly novel and not obvious in view of the prior art.

Moreover, the present invention as now recited in claim 3 (Currently Amended) is directed to a PDT method conducted during PTCA in which the PDT method is conducted from 0.5-6 hours after the PTCA and using a single administration of the e6

photosensitizing compound claimed. The prior art individually or in combination with each other fail to teach PDT conducted 0.5 – 6 hours after PTCA or PDT conducted after PTCA in which a single photosensitizing compound administration is conducted.

In order to further support Applicants' position, by this Amendment, Applicants have submitted a Rule 1.132 Declaration by Tsuneyuki Nagae (attached herewith as the Nagae Declaration). Further, in Attachment C in this Amendment, Applicants have provided a further detailed discussion distinguishing the prior art from the presently claimed invention (hereinafter Detailed Discussion).

Aizawa is directed only at a PDT therapy. PDT therapy is distinct from an angioplasty treatment and Aizawa is completely silent with regard to the application of its PDT method or any PDT method would be applicable for use in conjunction with angioplasty treatment. Therefore, Aizawa fails to provide any motivation for one of ordinary skill in the art to apply its PDT method for use with an angioplasty treatment such as PTCA. This is due in part to the fact that the PDT treatment of Aizawa is not directed at treating mechanical injury to a blood vessel but the use of PDT for atherosclerosis in mammals. Since the treatment of mechanical injury and the treatment of atherosclerosis are two distinct procedures, absent impermissive hindsight, one of ordinary skill in the art would not be motivated to combine a treatment for mechanical injury such as that to which the present invention is directed as well as Narciso, and the atherosclerosis treatment of Aizawa to make the presently claimed invention obvious (see Nagae Declaration paragraphs 4-7 and Detailed Discussion pages 1-5 and page 9, first full paragraph).

Narciso is directed to a procedure which comprises multiple administrations of a photosensitizing agent over of a 5-18 day period (see Narciso Abstract and cols. 2, 3 and 4). Irradiation of the photosensitizing agent is not conducted until after a final photosensitizing agent administration procedure is performed in a catheter inclusion step, the photosensitizing agent is administered for the final repeated time (see Nagae Declaration paragraph 6 and Detailed Discussion pages 5-8).

Contrary to the Examiner's allegation in the final Office Action, with reference to the original rejection of the first Office Action of September 22, 2004, Narciso, page 7, paragraph 2, does not teach PDT during PTCA. On the contrary, the PTCA procedure is conducted at least 5-18 days following the PDT procedure and requires multiple administration of a photosensitizing agent (see Nagae Declaration, paragraphs 6-7 and Detailed Discussion pages 5-10). Conducting PDT 5-18 days after PTCA does not anticipate, teach or suggest the claimed PDT method which is conducted during PTCA, e.g. 0.5 to 6 hours after the photosensitizing agent is administered, and thus, during PTCA as claimed.

Moreover, the present invention would not have been obvious to one of ordinary skill in the art as Aizawa and Narciso are directed to two distinct and divergent methods which would not suggest to one of ordinary skill in the art to combine their individual steps in a single therapeutic method as claimed. Aizawa uses an e6 compound to liberate cytotoxic singlet oxygen and to kill SMC cells. Narciso uses an e6 compound in a completely different way as a competitive inhibitor to inhibit a growth factor of injured SMC cells (see e.g. Nagae Declaration, paragraphs 5-7 and Detailed Discussion). Neither teaches or suggests the present method of treating a stenosed site using a

single administration of a photosensitizing agent and irradiation as claimed. The divergent mechanism of treatment of Aizawa and Narciso from the mechanism of treatment of the present invention fails to suggest the present method, which includes a single administration of photosensitizing agent and laser fluence, let alone, the effectiveness of the present method in treating restenosis.

Furthermore, the present method provides unexpected advantages and features not obvious from Aizawa and Narciso (Nagae Declaration paragraphs 8-20). That the inhibition of a restenosis of the blood vessel after the angioplasty procedure can be achieved with success according to the present method is entirely unexpected from the teachings of Aizawa and Narciso. Moreover, the combination of steps recited in Claim 3 (Currently Amended) which results in the successful inhibition of restenosis after an angioplasty procedure is unpredictable by one of ordinary skill in the art, even in view of Aizawa and Narciso, contrary to the Examiner's allegations in the second complete paragraph at page 3 of the final Office Action (See Nagae Declaration, paragraph 20).

The non-obviousness of the present invention is further evidenced by the unexpected results provided in the Specification as filed in the Examples, Table 1 (page 39) which summarizes the results of the Examples and as further discussed in the Nagae Declaration paragraphs 9-14. Further, in paragraphs 15-19 of the Nagae Declaration, Applicants have provided additional data of experiments carryed out in accordance with the present invention for restenosis inhibition using the method as recited in claim 3 (Currently Amended). The further experiments discussed in paragraphs 15-19 of the Nagae Declaration revealed that the intravenous administration of NPe6, at a dosage of 0.1-5 mg/kg and at a laser fluence of 1-10 J/cm^2 is sufficient

and effective to inhibit the restenosis of the blood vessel induced after angioplasty treatment.

Based on the foregoing, Applicants respectfully submit that the claims are not obvious in view of the prior art of record and therefore respectfully request that the rejection to claims 3 and 4 as being obvious in view of Aizawa and Narciso be withdrawn.

In view of the foregoing, Applicants respectfully submit that the present application is in condition for allowance.